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MERCK AND CO., INC			MOORE, SUSANNA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/540,784	Applicant(s) FRALEY, MARK E.	
	Examiner SUSANNA MOORE	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 37-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 37-39 and 43 is/are rejected.
- 7) ☒ Claim(s) 40-42 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's arguments, see Remarks, filed 9/17/2008, with respect to Office Action mailed 6/17/2008 have been fully considered. Some of the rejections have been withdrawn and others have been maintained. Thus, this is a Final Office Action. In summary, claims 37-43 are currently pending and under consideration.

Claim Objections

The objection of claim 37 because of the following informalities: the word "Unsubstituted" should be replaced with "unsubstituted" is **withdrawn** based on the amendments.

The objection of claims 40-42 as being dependent upon a rejected base claim is **withdrawn** based on the amendments.

Claims 40-42 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The rejection of claims 37, 38 and 43 under 35 U.S.C. 112, second paragraph, as being indefinite for the variables "a" and "b" are not defined on formula I is **withdrawn** based on the amendments.

The rejection of claims 37, 38 and 43 under 35 U.S.C. 112, second paragraph, as being indefinite for the definition of R^a and R^b is **withdrawn** based on the amendments.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37, 38 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The R^a and R^b substituents have been amended as "... b) ... or substituted C₁-C₆ alkyl, c) ... or substituted C₃-C₁₀ cycloalkyl." This is new matter since R^a and R^b can only be substituted with R^d. Furthermore, cycloalkyl was not previously defined as being substituted.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 37-39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bilodeau et. al. (US 6380203 B1).

The instant Application claims compounds of formula (I) as tyrosine kinase inhibitors, wherein R^2 , R^3 and R^5 = hydrogen, R^4 = 4-methoxyphenyl and R^1 = 5-methoxy-3-pyridyl).

The reference teaches compounds of formula (I) as tyrosine kinase inhibitors, wherein R^2 , R^3 and R^5 = hydrogen, R^4 = 4-methoxyphenyl and R^1 = 3-pyridyl, see column 10, example 1, lines 43-56.

The difference between the claimed compound and the reference is the substitution on the pyridyl at the 3-position of the bicycle, hydrogen versus Applicant's 5-methoxy. The genus of formula (I) in column 2, teaches that the heterocyclic ring at R^1 can be substituted with hydrogen, alkyl, mono- and dialkylamino, aryl, heterocyclyl, etc. See lines 56-65, in column. Furthermore, the genus also teaches R^1 can be alkyl, halo, alkenyl, alkynyl and heteroaryl substituted with COOalkyl, see column 2, lines 41-46. Thus, said claims are rendered obvious by Bilodeau et. al.

Applicant traverses the above rejection by stating, "... a closer inspection of the claimed invention will reveal that when R¹ is a C₅₋₁₀ heterocyclyl it must contain at least one substituent and that substituent cannot be a methoxy group. The substituents available for substitution on the C₅₋₁₀ heterocyclyl are significantly different both structurally and chemically from the compounds disclosed in Fraley et al. Thus, a person of ordinary skill in the art would not expect the instantly claimed compounds." This is not found persuasive because as mentioned above in the rejection, the genus teaching not only specifies a methoxy, the generic teaching in the reference teaches R¹ is alkyl, the same as claimed in the instant Application. Furthermore, there is significant overlap at R⁴, see column 2, line 50. Thus, the rejection is maintained.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Claims 37-39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bilodeau et. al. (US 6235741 B1). The 10th specie listed in claim 3 of the reference, 3-(3-pyridyl)-6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine is obvious over 3-(4-amino(3-pyridyl))-6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine. The only difference between the two named species is the substitution on the pyridyl ring at the 6-position of the bicycle, the amino substituent at the four position of the pyridyl ring claimed in the instant invention versus hydrogen. The genus in column 2, lines 56 and 59 teaches the variables are alternatively useable. The reference also teaches R¹ can be alkyl, alkenyl, alkynyl and heteroaryl substituted with COOalkyl, see column 2, lines 42-46 and 56-61. Thus, said claims are rendered obvious by the '741 patent.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the

reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 37, 38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bilodeau et. al. (US 6245759 B1). The 12th specie listed in claim 2 of the reference, 1-(3-dimethylamino-propyl)-4-(3-thiophen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one is obvious over (3-thiophen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one. The only difference between the two named species is the substitution on the pyridyl ring at the 6-position of the bicycle, the 3-dimethylamino-propyl versus Applicant's hydrogen. The genus in column 27, line 32, teaches the two variables are alternatively useable. Thus, said claims are rendered obvious by the '759 patent.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the

reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Claims 37, 38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeFeo-Jones et. al. (US 20020041880 A1).

The instant Application claims compounds of formula (I), wherein R^2 , R^3 and R^5 = hydrogen, R^4 = 4-methoxyphenyl and R^1 = alkyl and heterocyclyl substituted with a COOalkyl.

The reference teaches compounds of formula (I), wherein R^2 , R^3 and R^5 = hydrogen, R^4 = 4-methoxyphenyl and R^1 = thienyl. See page 46, example 1, bottom of left-hand column.

The only difference between the two named species is the substitution at R^1 , thienyl versus Applicant's alkyl and heterocyclyl substituted with a COOalkyl. The genus on page 6, left-hand column, paragraph 0056, 0060 and 0062. The genus in the reference teaches these variables are alternatively useable. This is just one example in the reference which renders the instant Application obvious. Thus, said claims are rendered obvious by DeFeo-Jones et. al.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or

declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

The above rejections all have common ownership. Applicant provided a statement in the remarks addressing the common ownership but this is not acceptable. The statement must be submitted as a declaration; thus must be submitted under 37 CFR 1.132 or 1.131 or 1.130, see the paragraph above. Thus, the rejections are maintained.

The rejection of claims 37, 38 and 43 under 35 U.S.C. 103(a) as being unpatentable over Bellec et. al. (J. of Heterocyclic Chemistry, 1995, 32(6), 1793-1800) is **withdrawn** based on the remarks by Applicant, there is not a specific or significant utility discussed in the reference.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

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application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37-39 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-3 of U.S. Patent No. 6235741. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '741 patent contains obvious variants of the species embraced by the genus of the instant Application. For example, the 10th specie listed in claim 3 of the reference, 3-(3-pyridyl)-6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine is obvious over 3-(4-amino(3-pyridyl))-6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine. The only difference between the two named species is the substitution on the pyridyl ring at the 6-position of the bicycle, the amino substituent at the

four position of the pyridyl ring claimed in the instant invention versus hydrogen. The genus in column 2, lines 56 and 59 teaches the variables are alternatively useable. Thus, said claims are rendered obvious by the '741 patent.

Applicant states, "The purpose of the doctrine of nonstatutory (obviousness-type) double patenting is to prevent issuance of a patent on claims that are not patentably distinct from the claims of an earlier patent. See *Eli Lilly & Co. v. Barr Laboratories*, 251 F.3d 955, 968 (Fed. Cir. 2001). Obviousness-type double patenting differs from obviousness under 35 USC 103 in that 103 obviousness compares the claimed subject matter to the prior art, while nonstatutory double patenting compares claims in an earlier patent to claims in a later patent application. *Geneva Pharm. Inc. v. Glaxosmithkline*, 349 F.3d 1373, 1378 (Fed. Cir. 2003). "Because nonstatutory double patenting compares earlier and later claims, an earlier patent's disclosure is not available to show nonstatutory double patenting." *Id.* at 1385. Thus, the Examiner's reference to the teaching of R1 as alkyl in the '741 patent disclosure is irrelevant to a nonstatutory double patenting rejection because R1 is not defined as alkyl in the claims of '741."

This is not found persuasive. The obviousness-type double patenting rejection must only render the claims obvious, hence the claims do not have to overlap. The reference teaches the substituents are alternatively useable. Thus, the rejection is maintained.

The obviousness-type double patenting rejection of claims 37, 38 and 43 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6245759 is **withdrawn** based on the amendments.

Claims 37-39 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-3 of U.S. Patent No. 6380203. Although the conflicting claims are not identical, they are not patentably distinct from each other for the same reason cited **in the 103 art rejection above.**

Applicant remarks, "In response, Applicants contend that the Examiner's conclusory statement is insufficient to give notice of the reasons for the rejection. MPEP 2141(g) states that an Examiner must support an obviousness rejection by articulating her findings regarding the Graham factors and explaining her conclusion of obviousness. "35 USC 132 requires that the applicant be notified of the reasons for the rejection of the claim so that he or she can decide how best to proceed." MPEP 2141(K). The Examiner's explanation "for the same. reason cited in the 103 art rejection above" does not give the Applicants notice of the factual basis for the rejection. The double patenting rejections based on '741 and '759 were based on specific comparisons of the instant claims to the prior patented claims. Since '741 and '759 claim patentably distinct species from those claimed in '203, it is not clear how the same reasoning can support a rejection over '203."

This is not found persuasive. The same argument cited above for the 103 rejection applies here. The rejection does not have to be repeated if it already appears in the office action. The same factors are weighed for a 103 art rejection as is for an obviousness-type rejection. Thus, the rejection is maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624
/Brenda L. Coleman/
Primary Examiner, Art Unit 1624